

We Claim:

1. A method for processing protein or peptide samples, comprising:
 - (i) reversibly immobilizing said peptide or protein samples onto a solid support;
 - (ii) transforming the immobilized peptide or protein by solid-phase chemical or enzymatic means, or a combination thereof;
 - (iii) eluting the resulting peptide- or protein-derived fragments from said solid support; and
 - (iv) recovering the fragments.
2. The method of claim 1, wherein the solid support is an ion-exchange resin.
3. The method of claim 2, wherein the resin is a cation exchange resin.
4. The method of claim 1, wherein the transformation is digestion of the peptide or protein.
5. The method of claim 4, wherein the digestion is carried out using an enzyme.
6. The method of claim 5, wherein the enzyme is trypsin.
7. The method of claim 2, where the immobilization and elution are pH-dependent.
8. The method of claim 2, where the immobilization and elution are ionic strength-dependent.
9. The method of claim 1, wherein the transformation is chemical transformation of the peptide or protein.
10. The method of claim 9, wherein the transformation is reduction of the peptide or protein.
11. The method of claim 9, wherein the transformation is alkylation of the peptide or protein.
12. The method of claim 11, wherein the transformation is alkylation of cysteine residues.
13. The method of claim 1, wherein the processing is carried out in semi-batch mode.
14. The method of claim 1, wherein the total peptide or protein amount is less than about 1 pmol.
15. The method of claim 14, wherein the total peptide or protein amount is less than about 100 fmol.
16. The method of claim 15, wherein the total peptide or protein amount is less than about 10 fmol.

17. The method of claim 16, wherein the total peptide or protein amount is less than about 1 fmol.
18. The method of claim 1, wherein the total peptide or protein amount is less than about 50ng.
- 5 19. The method of claim 1, wherein said sample is a complex mixture comprises at least about 10 different types of proteins or polypeptides.
20. The method of claim 1, wherein said fragments are suitable for use in mass spectrometer analysis.
21. The method of claim 1, further comprising washing said samples after step (i) with one
10 or more buffers before step (ii).
22. The method of claim 1, wherein said sample contains high concentrations of detergents and/or salts.
23. The method of claim 22, wherein the concentration of said salts is about 0.5M.
24. The method of claim 22, wherein the concentration of said detergent is about 1%.
- 15 25. The method of claim 1, further comprising dehydrating said protein or peptide samples on said solid support by purging all solvents used to dissolve said samples after step (i), followed by rehydrating said protein or peptide samples before step (ii).
26. The method of claim 25, wherein said dehydrating and rehydrating steps are separated by a period of storage time.
- 20 27. The method of claim 1, wherein said solid support is ion-exchange resin packed in a column.
28. The method of claim 27, wherein said resin is strong cation exchange resin.
29. The method of claim 1, wherein said protein or peptide is immunoprecipitated from a biological sample.
- 25 30. The method of claim 29, wherein said biological sample is a lysate of a cell expressing said protein or peptide.
31. The method of claim 1, wherein at least one of steps (i), (iii), or (iv) is facilitated by a solvent delivery system.

32. The method of claim 31, wherein said solvent delivery system is capable of delivering solvents to more than one independently operating solid supports.
33. A method of determining the ratio of proteins in a first and a second samples, the method comprising:
- 5 (a) processing said first sample using the method of claim 5 in the presence of H_2^{18}O , thereby labeling the carboxy termini of the peptide fragments resulting from the digestion with ^{18}O ;
- (b) processing said second sample using the method of claim 5 at the presence of H_2^{16}O , thereby labeling the carboxy termini of the peptide fragments resulting from the digestion with ^{16}O ;
- 10 (c) analyzing all peptide fragments of steps (a) and (b) using mass spectrometry by determining the ratio of each pair isotopically labeled fragment, thereby determining the ratio of proteins in said first and second sample.
34. An apparatus for processing protein or peptide samples according to claim 1, comprising:
- 15 (i) a reactor comprising a solid support;
- (ii) a solvent delivery system; and
- (iii) a means for connecting (i) and (ii).
35. A method for processing a cell sample of one or more cells, comprising:
- (i) introducing said cell sample into a cell harvest column,
- 20 (ii) washing said one or more cells,
- (iii) attaching a reactor column to said cell harvest column,
- (iv) lysing said cells,
- (v) reversibly immobilizing peptides or proteins resulting from the lysis onto a solid support;
- 25 (vi) transforming the immobilized peptide or protein by solid-phase chemical or enzymatic means, or a combination thereof;
- (vii) eluting the resulting peptide- or protein-derived fragments from said solid support; and
- (viii) recovering the fragments.
- 30 36. The method of claim 35, wherein said cell sample comprises no more than 1000 cells.
37. The method of claim 35, wherein said cell sample comprises no more than 100 cells.

38. The method of claim 35, wherein said cell sample comprises no more than 10 cells.
39. The method of claim 35, wherein said cell sample comprises a single cell.